



Oxidative stress impairs the heat stress response and delays unfolded protein recovery

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Abstract:

Background: Environmental changes, air pollution and ozone depletion are increasing oxidative stress, and global warming threatens health by heat stress. We now face a high risk of simultaneous exposure to heat and oxidative stress. However, there have been few studies investigating their combined adverse effects on cell viability. **Principal Findings:** Pretreatment of hydrogen peroxide (H₂O₂) specifically and highly sensitized cells to heat stress, and enhanced loss of mitochondrial membrane potential. H₂O₂ exposure impaired the HSP40/HSP70 induction as heat shock response (HSR) and the unfolded protein recovery, and enhanced eIF2 alpha phosphorylation and/or XBP1 splicing, land marks of ER stress. These H₂O₂-mediated effects mimicked enhanced heat sensitivity in HSF1 knockdown or knockout cells. Importantly, thermal preconditioning blocked H₂O₂-mediated inhibitory effects on refolding activity and rescued HSF1 +/+ MEFs, but neither blocked the effects nor rescued HSF1 -/- MEFs. These data strongly suggest that inhibition of HSR and refolding activity is crucial for H₂O₂-mediated enhanced heat sensitivity. **Conclusions:** H₂O₂ blocks HSR and refolding activity under heat stress, thereby leading to insufficient quality control and enhancing ER stress. These uncontrolled stress responses may enhance cell death. Our data thus highlight oxidative stress as a crucial factor affecting heat tolerance.

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Resource Description

Exposure :

weather or climate related pathway by which climate change affects health

Temperature

Temperature: Extreme Heat

Geographic Feature:

resource focuses on specific type of geography

None or Unspecified

Geographic Location:

resource focuses on specific location

Global or Unspecified

Climate Change and Human Health Literature Portal

Health Impact:

specification of health effect or disease related to climate change exposure

Injury, Other Health Impact

Other Health Impact: heat stress; oxidative stress

Resource Type:

format or standard characteristic of resource

Research Article

Timescale:

time period studied

Time Scale Unspecified